Personalized selective activation of γδT Vδ2 cells using zoledronic acid for glioblastoma *MICA/B^{high}* therapy: *in vitro* and *in vivo* investigations

Glioblastoma (GBM) is the most aggressive primary brain tumor in adults, with an average survival of only 15 months despite surgery, radiotherapy, and chemotherapy. A major obstacle in treating this cancer is its ability to suppress the immune system and avoid standard therapies. A new solution may come from an unusual group of immune cells: γδT Vδ2 cells. Unlike conventional T cells, they can recognize and attack tumors without requiring traditional signals, making them promising tools against glioblastoma.

This project explores a novel treatment approach utilizing unconventional **γδT Vδ2** lymphocytes, which, unlike classical lymphocytes, can recognize tumors without the need for MHC molecules. These cells will be collected from the patient blood and then activated and expanded in the laboratory using zoledronic acid and cytokines milieu personalized according to the phenotype of the patient's cells. To further increase tumor-killing power, the project will introduce a temporary genetic boost, instructing the cells to produce more **NKG2D** - a receptor that helps them detect cancer.

The efficacy of the therapy will first be evaluated *in vitro* on **patient-derived tumor organoids**, and subsequently *in vivo* in a **mouse model** where patient-derived tumors and immune cells will be combined.

The project is innovative because it avoids a one-size-fits-all approach. Instead, it adapts the therapy to each patient's unique immune landscape, addressing glioblastoma's heterogeneity. If successful, it could lead to a new class of personalized immunotherapies for brain cancer and beyond.